WHAT IS CLAIMED IS:

1. A method of selecting polynucleotides which encode an antigen-specific immunoglobulin molecule, or antigen-specific fragment thereof, comprising:

(a) introducing into a population of eukaryotic host cells capable of expressing said immunoglobulin molecule a first library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of first immunoglobulin subunit polypeptides, each first immunoglobulin subunit polypeptide comprising:

(i) a first immunoglobulin constant region selected from the group consisting of a heavy chain constant region and a light chain constant region,

(ii) an immunoglobulin variable region corresponding to said first constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said first immunoglobulin subunit polypeptide;

(b) introducing into said host cells a second library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of second immunoglobulin subunit polypeptides, each comprising:

(i) a second immunoglobulin constant region selected from the group consisting of a heavy chain constant region and a light chain constant region, wherein said second immunoglobulin constant region is not the same as said first immunoglobulin constant region,

(ii) an immunoglobulin variable region corresponding to said second constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said second immunoglobulin subunit polypeptide,

wherein said second immunoglobulin subunit polypeptide is capable of combining with said first immunoglobulin subunit polypeptide to form an immunoglobulin molecule, or antigen-specific fragment thereof, attached to the membrane surface of said host cells;

(c) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(d) contacting said immunoglobulin molecules with an antigen; and

(e) recovering those polynucleotides of said first library which express immunoglobulin molecules, or antigen-specific fragments thereof, specific for said antigen.

2. The method of claim 1, further comprising:

(f) introducing said recovered polynucleotides into a population of host cells capable of expressing said immunoglobulin molecule;

(g) introducing into said host cells said second library of polynucleotides;

(h) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(i) contacting said host cells with said antigen; and

(j) recovering those polynucleotides of said first library which express immunoglobulin molecules, or antigen-specific fragments thereof, specific for said antigen.

3. The method of claim 2, further comprising repeating steps (f)-(j) one or more times, thereby enriching for polynucleotides of said first library which encode a first immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

4. The method of claim 1, further comprising isolating those polynucleotides recovered from said first library.

5. The method of claim 4, further comprising:

(k) introducing into a population of eukaryotic host cells capable of expressing said immunoglobulin molecule said second library of polynucleotides;

(l) introducing into said host cells those polynucleotides isolated from said first library;

(m) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(n) contacting said host cells with said specific antigen; and

(o) recovering those polynucleotides of said second library which express immunoglobulin molecules, or antigen-specific fragments thereof, specific for said antigen.

6. The method of claim 5, further comprising:

(p) introducing said recovered polynucleotides into a population of host cells capable of expressing said immunoglobulin molecule;

(q) introducing into said host cells those polynucleotides isolated from said first library;

(r) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(s) contacting said host cells with said antigen; and

(t) recovering those polynucleotides of said second library which express immunoglobulin molecules, or antigen-specific fragments thereof, specific for said antigen.

7. The method of claim 6, further comprising repeating steps (p)-(t) one or more times, thereby enriching for polynucleotides of said second library which encode a second immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

8. The method of claim 7, further comprising isolating those polynucleotides recovered from said second library.

9. The method of claim 1, wherein said immunoglobulin molecule is a human immunoglobulin molecule.

10. The method of claim 1, wherein said first immunoglobulin subunit polypeptide is an immunoglobulin heavy chain, or antigen-specific fragment thereof.

11. The method of claim 10, wherein said immunoglobulin heavy chain, or antigen-specific fragment thereof, is a membrane bound form of an immunoglobulin heavy chain.

12. The method of claim 11, wherein said immunoglobulin heavy chain, or antigen-specific fragment thereof, comprises a naturally-occurring immunoglobulin transmembrane domain.

13. The method of claim 11, wherein said immunoglobulin heavy chain, or antigen-specific fragment thereof, is attached to said host cell as part of a fusion protein.

14. The method of claim 13, wherein said fusion protein comprises a heterologous transmembrane domain.

15. The method of claim 13, wherein said fusion protein comprises a fas death domain.

16. The method of claim 10, wherein said immunoglobulin heavy chain, or antigen-specific fragment thereof, is selected from the group consisting of an IgM heavy chain, an IgD heavy chain, an IgG heavy chain, an IgA heavy chain, an IgE heavy chain, and an antigen-specific fragment of any of said heavy chains.

17. The method of claim 10, wherein said immunoglobulin heavy chain constant region sequence comprises a modification that supports an altered immune effector function.

18. The method of claim 16, wherein said immunoglobulin heavy chain, or antigen-specific fragment thereof, comprises an IgM heavy chain, or an antigen specific fragment thereof.

19. The method of claim 1, wherein said second immunoglobulin subunit polypeptide is an immunoglobulin light chain, or antigen-specific fragment thereof.

20. The method of claim 19, wherein said immunoglobulin light chain, or antigen-specific fragment thereof, associates with said immunoglobulin heavy chain, or antigen-specific fragment thereof, thereby producing a immunoglobulin molecule, or antigen-specific fragment thereof.

21. The method of claim 19, wherein said immunoglobulin light chain is selected from the group consisting of a kappa light chain and a lambda light chain.

22. The method of claim 1, wherein said first library of polynucleotides is constructed in a eukaryotic virus vector.

23. The method of claim 1, wherein said second library of polynucleotides is constructed in a eukaryotic virus vector.

24. The method of claim 5, wherein said polynucleotides isolated from said first library are introduced by means of a eukaryotic virus vector.

25. The method of claim 1, wherein said second library of polynucleotides is constructed in a plasmid vector.

26. The method of claim 22, wherein said host cells are infected with said first library at an MOI ranging from about 1 to about 10, and wherein said second library is introduced under conditions which allow up to 20 polynucleotides of said second library to be taken up by each infected host cell.

27. The method of claim 5, wherein said polynucleotides isolated from said first library are introduced into said host cells in a plasmid vector.

28. The method of claim 22, wherein said eukaryotic virus vector is an animal virus vector.

29. The method of claim 23, wherein said eukaryotic virus vector is an animal virus vector.

30. The method of claim 28, wherein said virus vector is capable of producing infectious viral particles in mammalian cells.

31. The method of claim 30, wherein the naturally-occurring genome of said virus vector is DNA.

32. The method of claim 30, wherein the naturally-occurring genome of said virus vector is RNA.

33. The method of claim 31, wherein the naturally-occurring genome of said virus vector is linear, double-stranded DNA.

34. The method of claim 33, wherein said virus vector is selected from the group consisting of an adenovirus vector, a herpesvirus vector and a poxvirus vector.

35. The method of claim 34, wherein said virus vector is a poxvirus vector.

36. The method of claim 35, wherein said poxvirus vector is selected from the group consisting of an orthopoxvirus vector, an avipoxvirus vector, a capripoxvirus vector, a leporipoxvirus vector, an entomopoxvirus vector, and a suipoxvirus vector.

37. The method of claim 36, wherein said poxvirus vector is an orthopoxvirus vector selected from the group consisting of a vaccinia virus vector and a raccoon poxvirus vector.

38. The method of claim 37, wherein said animal virus vector is a vaccinia virus vector.

39. The method of claim 38, wherein said host cells are permissive for the production of infectious viral particles of said virus.

40. The method of claim 38, wherein said vaccinia virus is attenuated.

41. The method of claim 40, wherein said vaccinia virus vector is deficient in D4R synthesis.

42. The method of claim 35, wherein said transcriptional control region of said first library of polynucleotides functions in the cytoplasm of a poxvirus-infected cell.

43. The method of claim 25, wherein said plasmid vector directs synthesis of said second immunoglobulin subunit in the cytoplasm of a poxvirus-infected cell through operable association with a transcription control region.

44. The method of claim 42, wherein said transcriptional control region comprises a promoter.

45. The method of claim 44, wherein said promoter is constitutive.

46. The method of claim 45, wherein said promoter is a vaccinia virus p7.5 promoter.

47. The method of claim 45, wherein said promoter is a synthetic early/late promoter.

48. The method of claim 44, wherein said promoter is a T7 phage promoter active in cells in which T7 RNA polymerase is expressed.

49. The method of claim 42, wherein said transcriptional control region comprises a transcriptional termination region.

50. The method of claim 22, wherein said first library of polynucleotides is constructed in a eukaryotic virus vector by a method comprising:

(a) cleaving an isolated linear DNA virus genome to produce a first viral fragment and a second viral fragment, wherein said first fragment is nonhomologous with said second fragment;

(b) providing a population of transfer plasmids comprising said polynucleotides which encode said plurality of immunoglobulin heavy chains through operable association with a transcription control region, flanked by a 5' flanking region and a 3' flanking region, wherein said 5' flanking region is homologous to said first viral fragment and said 3' flanking region is homologous to said second viral fragment; and wherein said transfer plasmids are capable of homologous recombination with said first and second viral fragments such that a viable virus genome is formed;

(c) introducing said transfer plasmids and said first and second viral fragments into a host cell under conditions wherein a transfer plasmid and said viral fragments undergo *in vivo* homologous recombination, thereby

producing a viable modified virus genome comprising a polynucleotide which encodes an immunoglobulin heavy chain; and

(d) recovering said modified virus genome.

51. The method of claim 23, wherein said second library of polynucleotides is constructed in a eukaryotic virus vector by a method comprising:

(a) cleaving an isolated linear DNA virus genome to produce a first viral fragment and a second viral fragment, wherein said first fragment is nonhomologous with said second fragment;

(b) providing a population of transfer plasmids comprising said

polynucleotides which encode said plurality of immunoglobulin light chains through operable association with a transcription control region, flanked by a 5' flanking region and a3' flanking region, wherein said 5' flanking region is homologous to said first viral fragment and said 3' flanking region is homologous to said second viral fragment; and wherein said transfer plasmids are capable of homologous recombination with said first and second viral fragments such that a viable virus genome is formed;

(c) introducing said transfer plasmids and said first and second viral fragments into a host cell under conditions wherein a transfer plasmid and said viral fragments undergo *in vivo* homologous recombination, thereby producing a viable modified virus genome comprising a polynucleotide which encodes an immunoglobulin light chain; and

(d) recovering said modified virus genome.

52. The method of claim 1, wherein said polynucleotides encoding antigen-specific immunoglobulin molecules are identified through detection of an effect selected from the group consisting of:

(a) antigen-induced cell death;

(b) antigen-induced signaling; and

(c) antigen-specific binding.

53. The method of claim 5, wherein said polynucleotides encoding antigen-specific immunoglobulin molecules are identified through detection of an effect selected from the group consisting of:

(a) antigen-induced cell death;

(b) antigen-induced signaling; and

(c) antigen-specific binding.

54. The method of claim 52, wherein said effect is antigen-induced cell death.

55. The method of claim 53, wherein said effect is antigen-induced cell death.

56. The method of claim 54, wherein said host cells express immunoglobulin molecules on their surface, and wherein said host cells expressing immunoglobulin molecules which bind said antigen directly respond to cross-linking of antigen-specific immunoglobulin receptors by induction of apoptosis.

57. The method of claim 55, wherein said host cells express immunoglobulin molecules on their surface, and wherein said host cells expressing immunoglobulin molecules which bind said antigen directly respond to cross-linking of antigen-specific immunoglobulin receptors by induction of apoptosis.

58. The method of claim 52, wherein said effect is antigen-induced signaling.

59. The method of claim 53, wherein said effect is antigen-induced signaling.

60. The method of claim 58, wherein said host cells express immunoglobulin molecules on their surface, and wherein said host cells expressing immunoglobulin molecules which bind said antigen respond to cross-linking of antigen-specific immunoglobulin receptors by expression of a detectable reporter molecule.

61. The method of claim 59, wherein said host cells express immunoglobulin molecules on their surface, and wherein said host cells expressing immunoglobulin molecules which bind said antigen respond to cross-linking of antigen-specific immunoglobulin receptors by expression of a detectable reporter molecule.

62. The method of claim 60, wherein said reporter molecule is selected from the group consisting of luciferase, green fluorescent protein, and beta-galactosidase.

63. The method of claim 61, wherein said reporter molecule is selected from the group consisting of luciferase, green fluorescent protein, and beta-galactosidase.

64. The method of claim 52, wherein said effect is antigen-specific binding.

65. The method of claim 64, comprising:

(a) contacting pools of said host cells with said antigen under conditions wherein antigen-specific immunoglobulin molecules expressed by said host cells will bind to said antigen; and

(b) recovering polynucleotides of said first library from those host cell pools, or from replicate pools of polynucleotides set aside previously, expressing immunoglobulin molecules to which said antigen was bound.

66. The method of claim 65, further comprising:

(c) dividing said recovered polynucleotides into a plurality of sub-pools and introducing said sub-pools into populations of host cells capable of expressing said immunoglobulin molecule;

(d) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(e) contacting said pools with said antigen under conditions wherein antigen-specific immunoglobulin molecules expressed by said host cells bind to said antigen; and

(f) recovering polynucleotides of said first library from those host cell pools, or from replicate pools of polynucleotides set aside previously, expressing immunoglobulin molecules to which said antigen was bound.

67. The method of claim 66, further comprising repeating steps (c)-(f) one or more times, thereby enriching for polynucleotides of said first library which encode a first immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

68. The method of claim 64, wherein said antigen is attached to a substrate selected from the group consisting of a synthetic particle, a polymer, a magnetic bead, and a protein-coated tissue culture plate.

69. The method of claim 64, wherein said antigen is expressed on the surface of an antigen-expressing presenting cell, wherein said antigen-expressing presenting cell is constructed by transfecting an antigen-free presenting cell with a polynucleotide which operably encodes said antigen.

70. The method of claim 69, wherein said antigen-expressing presenting cell is constructed in an antigen-free presenting cell selected from the group consisting of an L cell, a Cos7 cell, a 293 cell, a HeLa cell, and an NIH 3T3 cell.

71. The method of claim 65, wherein said antigen is conjugated to a fluorescent tag, and wherein host cell pools expressing immunoglobulin molecules which bind antigen are identified through fluorescence activated cell sorting.

72. The method of claim 53, wherein said effect is antigen-specific binding.

73. The method of claim 72, comprising:

(a) contacting pools of said host cells with said antigen under conditions wherein antigen-specific immunoglobulin molecules expressed by said host cells will bind to said antigen; and

(b) recovering polynucleotides of said second library from those host cell pools, or from replicate pools of polynucleotides set aside previously, expressing

immunoglobulin molecules to which said antigen was bound.

74. The method of claim 73, further comprising:

(c) dividing said recovered polynucleotides into a plurality of sub-pools and introducing said sub-pools into populations of host cells capable of expressing said immunoglobulin molecule;

(d) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(e) contacting said pools with said antigen under conditions wherein antigen-specific immunoglobulin molecules expressed by said host cells bind to said antigen; and

(f) recovering polynucleotides of said second library from those host cell pools, or from replicate pools of polynucleotides set aside previously, expressing immunoglobulin molecules to which said antigen was bound.

75. The method of claim 74, further comprising repeating steps (c)-(f) one or more times, thereby enriching for polynucleotides of said first library which encode a first immunoglobulin subunit polypeptide which, as part of an immunoglobulin molecule, or antigen-specific fragment thereof, specifically binds said antigen.

76. The method of claim 72, wherein said antigen is attached to a substrate selected from the group consisting of a synthetic particle, a polymer, a magnetic bead, and a protein-coated tissue culture plate.

77. The method of claim 72, wherein said antigen is expressed on the surface of an antigen-expressing presenting cell, wherein said antigen-expressing

presenting cell is constructed by transfecting an antigen-free presenting cell with a polynucleotide which operably encodes said antigen.

78. The method of claim 77, wherein said antigen-expressing presenting cell is constructed in an antigen-free presenting cell selected from the group consisting of an L cell, a Cos7 cell, a 293 cell, a HeLa cell, and an NIH 3T3 cell.

79. The method of claim 73, wherein said antigen is conjugated to a fluorescent tag, and wherein host cell pools expressing immunoglobulin molecules which bind antigen are identified through fluorescence activated cell sorting.

80. A kit for the selection of antigen-specific recombinant immunoglobulins expressed in a eukaryotic host cell comprising:

(a) a first library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of first immunoglobulin subunit polypeptides, each first immunoglobulin subunit polypeptide comprising:

(i) a first immunoglobulin constant region selected from the group consisting of a heavy chain constant region and a light chain constant region,

(ii) an immunoglobulin variable region corresponding to said first constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said first immunoglobulin subunit polypeptide,

wherein said first library is constructed in a eukaryotic virus vector;

(b) a second library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of second immunoglobulin subunit polypeptides, each comprising:

(i) a second immunoglobulin constant region selected from the group consisting of a heavy chain constant region and a light chain constant region, wherein said second immunoglobulin constant region is not the same as said first immunoglobulin constant region,

(ii) an immunoglobulin variable region corresponding to said second constant region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said second immunoglobulin subunit polypeptide,

wherein a said second immunoglobulin subunit polypeptide is capable of combining with said first immunoglobulin subunit polypeptide to form a surface immunoglobulin molecule, or antigen-specific fragment thereof, and wherein said second library is constructed in a eukaryotic virus vector; and

(c) a population of host cells capable of expressing said immunoglobulin molecules;

wherein said first and second libraries are provided both as infectious virus particles and as inactivated virus particles, and wherein said inactivated virus particles infect said host cells and allow expression of said first and second immunoglobulin subunit polypeptides, but do not undergo virus replication; and

wherein antigen-specific immunoglobulin molecules expressed by said host cells are selected through interaction with an antigen.

81. An antibody, or antigen-specific fragment thereof, produced by the method of claim 1.

82. A composition comprising the antibody of claim 81, and a pharmaceutically acceptable carrier.

83. A method of selecting polynucleotides which encode a single-domain antigen-specific immunoglobulin molecule, or antigen-specific fragment thereof, comprising:

(a) introducing into a population of eukaryotic host cells capable of expressing said immunoglobulin molecule a library of polynucleotides encoding, through operable association with a transcriptional control region, a plurality of single-domain immunoglobulin polypeptides, each immunoglobulin polypeptide comprising:

(i) an immunoglobulin heavy chain constant region,

(ii) an camelized immunoglobulin heavy chain variable region, and

(iii) a signal peptide capable of directing cell surface expression or secretion of said immunoglobulin subunit polypeptide;

(b) permitting expression of immunoglobulin molecules, or antigen-specific fragments thereof, from said host cells;

(c) contacting said immunoglobulin molecules with an antigen; and

(d) recovering polynucleotides of said library from those host cells expressing immunoglobulin molecules which bind said antigen.